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Canadian Association of Radiologists Journal 64 (2013) 253–257

CANADIAN ASSOCIATION OF RADIOLOGISTS JOURNAL

www.carjonline.org

Neuroradiology / Neuroradiologie

The Use of Dynamic Computed Tomographic Angiography Ancillary to the Diagnosis of Brain Death

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Abstract

Objective: Global absence of cerebral circulation is an important ancillary test for brain death when the diagnosis cannot be confirmed clinically. A number of imaging methods are available to assess cerebral circulation; however, new techniques are sought to improve on limitations of the current tests. Dynamic computed tomographic angiography (dCTA) is a novel technique that enables dynamic noninvasive imaging of cerebral blood flow.
Materials and Methods: We present the use of dCTA in 3 cases as a corroboratory tool to diagnose brain death. Analysis of our findings suggest that it is a reliable technique for demonstrating the lack of intracranial blood flow, with many advantages over other current methods.
Conclusion: A dCTA may be used to reliably demonstrate the lack of cerebral blood flow in patients with suspected brain death.

Résumé

Objectif : La démonstration de l'absence globale de circulation intracrânienne est un test complémentaire important pour établir le diagnostic de mort cérébrale. Bien que plusieurs méthodes d'imagerie permettent déjà d'étudier la circulation cérébrale, de nouvelles techniques sont étudiées afin de repousser les limites des examens actuels. Ainsi, l'angioscanner dynamique (ATDM dynamique) est une technique récente non invasive qui permet d'obtenir des images dynamiques de la circulation sanguine cérébrale.
Matériel et méthode : Nous présentons l'utilisation de l'ATDM dynamique pour confirmer le diagnostic de mort cérébrale chez trois patients. L'analyse des résultats révèle que cette technique est fiable pour démontrer l'absence de circulation intracrânienne tout en offrant des avantages qui, à bien des égards, dépassent ceux des autres méthodes couramment employées.
Conclusion : L'ATDM dynamique peut être utilisée pour démontrer de façon fiable l'absence de circulation intracrânienne chez les patients suspects de mort cérébrale.

Neurologic determination of death (NDD), or brain death, is primarily considered a clinical diagnosis. However, ancillary testing is sometimes required in situations in which clinical assessment is impossible or confounded [1,2]. The diagnosis should be determined as early as possible to avoid unnecessary treatment and to allow organ harvesting for transplantation. Demonstration of the global absence of cerebral blood flow (CBF) is considered the standard for NDD by ancillary testing [3]. Among CBF imaging techniques, HMPAO SPECT (hexamethylpropylene amine oxime–single photon emission computed tomography) radionuclide angiography and 4-vessel cerebral angiography (CA) are the only examinations validated worldwide for use as ancillary tests in the determination of brain death. In Canada, however, computed tomography (CT) and magnetic

Key Words: Critical care; Diagnostic test assessment; Computed tomography; Brain death; Dynamic computed tomographic angiography.

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http://dx.doi.org/10.1016/j.carj.2012.04.005

resonance angiography (MRA) as well as xenon CT are acknowledged as ancillary tests [3]. Due to the limitations of the standard techniques, efforts have been made to evaluate alternative examinations as potential replacement tests.

With the advent of the 320-slice whole brain CT scanner, we are able to get whole brain CT perfusion data. From the same data set, dynamic (time-resolved) CT angiography (dCTA) images could be reconstructed, which enables us to analyse the blood flow in the entire cranial circulation in a noninvasive way with high spatial and temporal resolution [4]. Here, we present 3 cases in which dCTA was used as a corroboratory tool to diagnose brain death.

dCTA Protocol

A dCTA of the whole brain was performed with a 320-row volume CT scanner (Aquilion ONE, Toshiba, Japan). This system uses 320 ultrahigh resolution detector rows (0.5 mm in width) with 16-cm coverage to image the entire brain in a single gantry rotation. However, other CT vendors are developing comparable technologies to increase coverage of CT perfusion (eg, the helical volume shuttle technique), and the same data could also be used to generate dCTA images. Compared with older-generation CT scanners that are able to monitor either a small area of brain (a few slices of approximately 2-4 cm) during the time course of contrast flow or whole brain volume in predetermined time interval (snapshot views: standard CTA), the dCTA technique can monitor the contrast flow of the whole head (intra- and extracranial) during the total scanning time (80 seconds in brain death protocol). The predetermined time interval for the older CT scanner is often unreliable due to the changed or delayed cerebral flow in these patients. A dCTA eliminates the guesswork of timing of the CTA because it monitors the flow of contrast in cerebral vasculature during the whole scanning period (Figure 1). A dCTA is a noninvasive technique that could show us bone subtracted or nonsubtracted CTA images of the whole brain in multiple time points, which provides temporal flow information. In our brain death imaging protocol, whole brain imaging is performed once at 7 seconds (used as a mask for subtraction) from the start of injection of contrast; then every 2 seconds from 11-35 seconds (13 volumes), followed by a whole brain scan every 5 seconds up to 80 seconds (9 volumes) after the initial contrast bolus (Figure 1). Only 40 mL of intravenous contrast is used. Radiation dose for this study is 5.3 mSv, which is similar to 2 years of background radiation.

In all cases discussed below, a CTA was requested by the intensive care unit staff or by the treating physicians as an ancillary tool for the diagnosis of brain death due to the presence of confounding factors. The decision to switch from conventional single-phase CTA to dCTA was made by consciences based on our experience in using dynamic CTA in stroke imaging and our knowledge of its utility to provide dynamic blood flow information.

Case Reports

Case 1

A 17-year-old boy was found in his room without vital signs and was brought to the emergency department by paramedics, where he was found to be in severe metabolic acidosis subsequent to presumed overdose of narcotics. Diffuse brain oedema and pseudo-subarachnoid hemorrhage were observed in noncontrast CT (Figure 2A, B), which was suggestive of diffuse anoxic encephalopathy. Clinical assessment for brain death was confounded by narcotic ingestion and, therefore, ancillary testing was required. By using dCTA, delayed filling of the internal carotid arteries (ICA) and basilar arteries was observed in association with absent blood flow to the distal intracranial artery branches (Figure 2). At 10 seconds, contrast filling started in the external carotid–scalp branches (Figure 2C), contrast is seen in ICA at 12 seconds with very slow flow of contrast only to the skull base. Slow flow of contrast was noted in the basilar artery starting at 22 seconds. The extracranial branches completely washed out of contrast by 26 seconds. Only trickle flow of contrast was noted in the M1 segments at 28 seconds (Figure 2D). The contrast from the proximal ICA and basilar arteries drained out at 40 seconds. No contrast flow into the

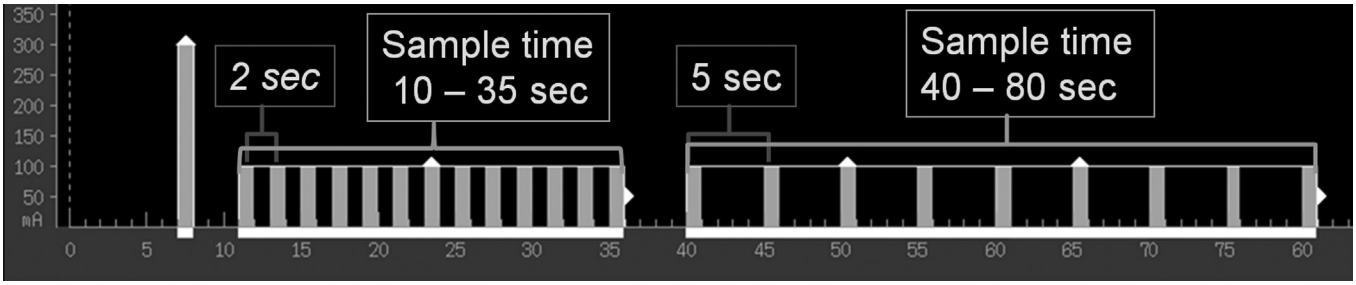

Figure 1. The timing diagram explains the acquisition of whole brain volumes at each time point starting at 7 seconds from the time of the start of contrast injection. This volume uses 300 mA and is used as a mask for subtraction. Next in the arterial phase (10-35 seconds), whole brain volumes are acquired every 2 seconds. In the venous phase (40-80 seconds), volumes are acquired at 5-second intervals. By using each individual or all volumes, we could assess flow of contrast in intra- and extracranial circulation during the whole scanning duration (80 seconds). In contrast, older computed tomography scanners could only obtain a snapshot view of the brain circulation at a predetermined time point, which could miss the contrast, depending on the circulation time in an individual patient.

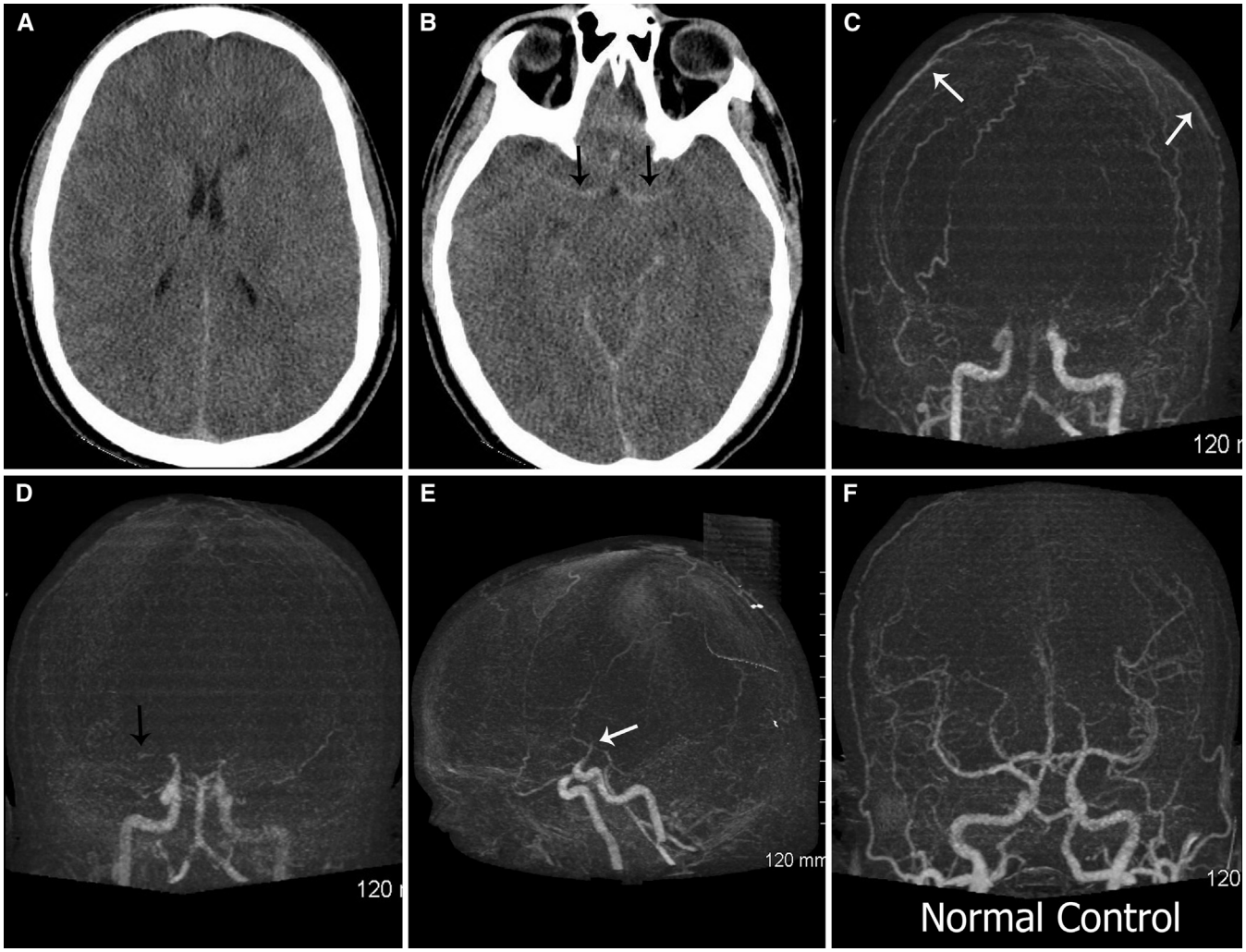

Figure 2. (A, B) Noncontrast computed tomography (CT) of the head, showing subtle loss of grey-white matter differentiation, brain swelling (A), and pseudo-subarachnoid hemorrhage (B) (black arrows). (C) Frontal view dynamic CT angiography at 24 seconds, showing delayed filling of the basilar artery and bilateral internal carotid arteries (ICA) at the skull base but no filling of the distal branches. Filling of the superficial temporal and external carotid branches (white arrows) are noted, which is helpful as an internal reference. (D) Frontal view at 28 seconds, showing minimal filling of the right M1 segment (black arrow) and no filling of the bilateral distal middle cerebral artery and posterior cerebral artery branches. (E) A lateral view at 24 seconds, showing abrupt tapering of the ICAs at the skull base (white arrow), a typical angiographic feature of brain death. (F) A normal control with simultaneous filling of intra- and extracranial branches.

more distal intracranial branches was noted during the whole acquisition, nor was there any opacification of the deep cerebral venous system (internal cerebral veins and the Galen vein), which confirmed a lack of cerebral flow, thus brain death, with no chance of recovery. The toxicology screen was positive for narcotics. Despite aggressive therapy, the patient continued to show evidence of multisystem organ failure, with refractory shock; hypoxemic respiratory failure; fulminant shock, with an extremely elevated liver enzyme values; and renal failure. His family elected to withdraw life support and arrangements for selective (bone and heart valves) organ donation were initiated pending the coroner's autopsy.

Case 2

A 52-year-old man with diabetes was admitted to neurosurgery for an elective laminectomy and resection of a sacral arachnoid cyst. After surgery, he had postoperative cardiac arrest complicated by a myocardial infarction and hyperkalemia. A CT of the head revealed diffuse oedema and ischemic change suggestive of hypoxic brain damage. The following morning, clinical assessment found no brain stem activity but did see evidence of spinal reflexes. For this reason, dCTA was requested to confirm the diagnosis of brain death. Noncontrast CT (Figure 3A) showed diffuse loss of grey matter density lower than the white matter, the so called reversal sign, a sign of diffuse ischemia. A dCTA demonstrated filling of the external carotid artery (ECA) branches (starting at 16 seconds and washing out by 30 seconds) but no filling of the ICAs, the anterior and middle cerebral arteries (MCAs), or the basilar artery (Figure 3B). At 60 seconds (Figure 3C), there was meager contrast flow noted in the right ICA only to the level of the skull base. Repeated clinical evaluation confirmed the absence of all brain stem

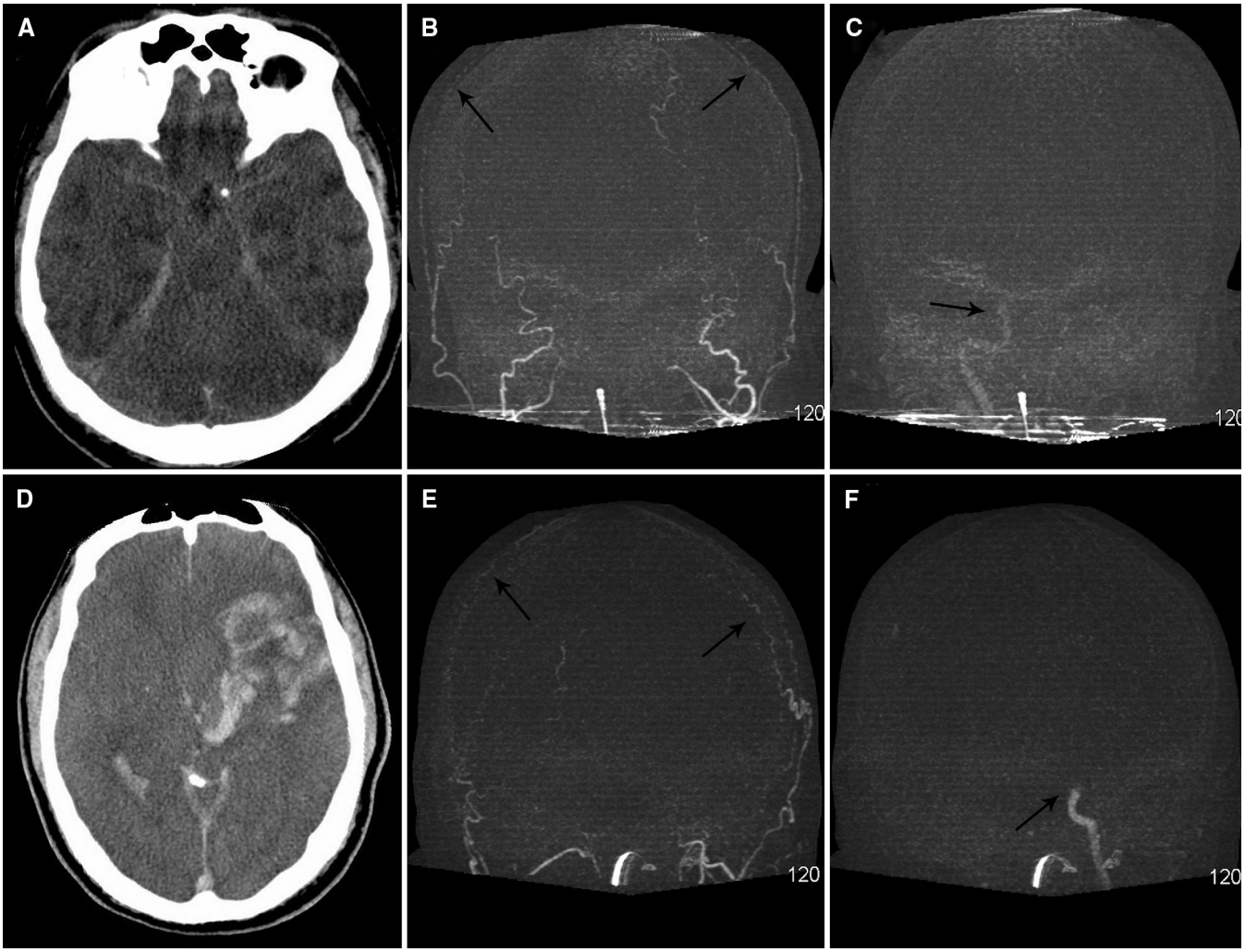

Figure 3. (A-C) Case 2. (A) Noncontrast computed tomography (CT), showing evidence of pseudosubarachnoid hemorrhage with ''reversal sign'' of grey matter hypodensity. (B) Dynamic CT angiography at 22 seconds, showing good flow in the external carotid branches to the level of vertex (black arrows) but no evidence of flow in internal carotid arteries (ICA) and intracranial branches. (C) At 60 seconds, there was meager contrast flow noted in the right ICA only to the level of the skull base (black arrow); please note the scalp arteries have completely cleared of contrast. (D-F) Case 3. (D) Noncontrast CT of the head, showing evidence of subacute infarction, with hemorrhagic transformation, intraventricular hemorrhage, and mass effect; subtle loss of grey-white matter differentiation was noted. (E) Dynamic CT angiography at 28 seconds, showing filling of the scalp arteries (black arrows) without any intracranial branches. (F) Delayed image at 70 seconds, showing contrast filling in the left ICA to the level of the cavernous segment (black arrow); intracranial blood flow is absent.

and spinal reflexes, with no confounding factors, and he was declared brain dead. The patient was removed from life support, and his organs were donated as per his family's wishes.

Case 3

A 58-year-old man presented to the emergency department with acute aphasia and left-sided paralysis. He had a history of diabetes, hypertension, and newly diagnosed atrial fibrillation. A CT demonstrated ischemic changes consistent with acute left MCA infarction and embolic occlusion of the left M1 segment. He was treated promptly with intravenous tissue plasminogen activator. The following morning, his level of consciousness decreased, and he was intubated and admitted to the intensive care unit. A repeat CT revealed extensive hemorrhagic conversion with intraventricular extension. Two days later, clinical evaluation showed findings consistent with deep coma and loss of brainstem reflexes. The patient's oxygen saturation had dropped significantly during the apnea test and, therefore, ancillary testing was requested. A dCTA was performed. A noncontrast CT of the head (Figure 3D) showed evidence of subacute infarction with hemorrhagic transformation in the left MCA territory, intraventricular hemorrhage, and mass effect with midline shift. Subtle loss of grey-white matter differentiation was also noted. In the dCTA, at approximately 20 seconds from the injection, contrast filling started at the left superficial temporal artery, left occipital artery, and other left ECA branches. The right ECA branches started filling at 22 seconds, with all ECA branches cleared out of contrast by 40 seconds. It is noted that there was no ICA filling at this time. At approximately 45 seconds, there was filling of the cervical and petrous portion of the left ICA, which continued

until 80 seconds. However, there was no evidence of flow above the level of the skull base in the left ICA at 80 seconds. No right ICA, vertebral, basilar, or deep venous flow was seen. The findings were consistent with absent CBF. A diagnosis of brain death was established and organ donation procedures were commenced.

Discussion

To the best of our knowledge, this article is the first reported use of dCTA to confirm the diagnosis of brain death. Potential applications for dCTA in stroke, steno- occlusive disease, arteriovenous malformations, and dural shunts have been reported [4]. The 3 case reports presented here suggest that dCTA may play a larger role as an ancillary test for NDD. There are a number of imaging methods currently available to assess CBF and perfusion. In clinical practice, electroencephalography, cerebral angiography, nuclear scan, HMPAO SPECT, transcranial Doppler, CTA, and magnetic resonance imaging−MRA are all currently used as ancillary tests for NDD in adults [2]. Cerebral circulatory arrest occurs when the intracranial pressure exceeds arterial inflow pressure. According to the Canadian recommendations for NDD, the acknowledged ancillary tests are catheter cerebral angiography, radionuclide angiography, CTA, MRA, and xenon CT [1].

A 4-vessel cerebral angiography remains the criterion standard despite being invasive, time consuming, and relatively expensive. However, recent advances in temporal and spatial resolution have allowed other techniques, for example, dCTA, to challenge this position. The accuracy of standard CTA was first shown to be excellent [5]; however, newer studies have reported intracranial vessel opacification in a substantial number of patients (11%-48%) [6,7], mainly in the proximal branches, thus doubting the utility of standard CTA as an ancillary test.

A dCTA has the advantage of providing visualization of dynamic blood flow information in contrast to traditional CTA, which makes it possible to analyse the pattern of flow qualitatively. Therefore, even in presence of minimal flow of small amount of contrast in the basal arteries (as in case 1), we are still confident to diagnose a lack of global intracranial flow. It also images the entire cranial vasculature simultaneously and allows comparison with the extracranial arterial flow that can be used as an internal control.

Aside from the intravenous contrast injection, it is a noninvasive and safe technique. It is considerably less time consuming and technically less demanding than cerebral angiography for both patients and radiologists, thereby permitting earlier determination of brain death and potentially expediting organ donation. This technique is becoming increasingly accessible because it is fairly inexpensive and other CT vendors have also developed alternative methods capable of performing whole brain CT perfusion. These perfusion data are also capable of generating whole brain dCTA and so could be used in a similar fashion.

In cases of brain death, CT perfusion map calculations are difficult due to a lack of reliable arterial input function determination and thus are not recommended. However, by using the same data, reconstructing dCTA images does not depend on any mathematical calculation and provides direct visualization of the blood flow. We must stress that, as with catheter cerebral angiogram, radiologists reporting time-resolved dCTA images in patients who are brain dead could only comment on the presence or absence of cerebral flow but not directly about brain death. Compared with catheter angiography, dCTA does have the ability of showing not just the lumen of the vessel but also other intracranial structures. Further longitudinal studies will be required to determine the sensitivity and specificity of this test in patients with clinical suspicion of brain death. The lack of a criterion standard comparison technique (such as angiography) in this case series is certainly a drawback in this project that would have been helpful in further validating the technique.

Conclusion

The cases presented here suggest that dCTA may be used to reliably demonstrate the lack of CBF in patients with suspected brain death. Further efforts should be made to evaluate and validate dCTA in this context.

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